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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,218	11/30/2001	Lonnie O'Neal Ingram	49950-59824CON4	1895

7590 04/16/2004
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EXAMINER

SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/001,218	Applicant(s) INGRAM ET AL.	
	Examiner Tekchand Saidha	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-12 and 14-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-12 and 14-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment filed January 27, 2004 in response to Office Action mailed February 8, 2000, is acknowledged. Claims 4, 13 & 18 have been canceled by this amendment. Claims 1-3, 5-12 and 14-17 are pending and under consideration in this examination.
2. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).
3. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.
4. Information Disclosure Statement (PTO-1449) filed January 27, 2004, is acknowledged. A signed copy of PTO-1449 is enclosed herewith.

5. ***Enablement***

Claims 1-3, 6-12 & 15-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for recombinant strain of *Bacillus subtilis* YB886 (pLOI1500) transformed with alcohol dehydrogenase (ADHII) and pyruvate decarboxylase (PDC) genes from *Zymomonas mobilis*, does not reasonably provide enablement for any eukaryotic cell or a method for ethanol production, including any animal cell, insect cell, or fungal cell transformed with genes encoding alcohol dehydrogenase (ADHII) and pyruvate decarboxylase (PDC), or polysaccharase(s) gene(s) to produce sufficient levels of ethanol as a fermentation product (claims 1-3, 6-

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12 & 17) and further develop a method of transforming any eukaryotic cell with a gene encoding any enzyme which would degrade oligosaccharides (claims 15-16).

The specification provides the example of recombinant strain of *Bacillus subtilis* YB886 (pLOI1500) transformed with ADHII and PDC activities. The specification describes 1 species and 2 strains of *Bacillus* (page 22, lines 2-5) after testing several species and strains as alternate hosts, which is an indication that not all species or strains within the same genera can so easily be transformed with the disclosed genes. Given the unpredictability shown above, extrapolating the guidance provided in the instant specification to be able to (a) express the alcohol dehydrogenase and pyruvate decarboxylase or polysaccharase(s) gene(s) obtained from any source and its expression in any eukaryotic cell system in sufficient levels would require guidance to (b) obtaining the genes from any source, many uncharacterized as yet, (c) optimizing the compatibility of such an expression system, i.e., whether a eukaryotic cell, such as from an insect, fungi or animal permit such a transformation of the genes for sufficient ethanol production, from excess of the product may prove toxic or detrimental to the cell system in question, which may be due to the lack of tolerance to higher levels of ethanol. Other bacteria, for example, *E. coli*, when transformed with genes coding for pyruvate decarboxylase and aldehyde dehydrogenase does not tolerate greater than 7.5% ethanol, as is well known in the art. (d) Guidance is also lacking about the transformation of the fermentative genes [alcohol dehydrogenase (ADHII) and pyruvate decarboxylase (PDC) or polysaccharase(s) gene(s)] into non-fermentative cell types, such as insect or animals or fungi, lack of which may result in non-viable constructs

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from producing ethanol any levels. (e) Adequate guidance to sustaining growth conditions or culture medium required for such a diverse group of cultures is also lacking, and no such conditions are described that would adequately support the transformants of varying eukaryotic cell types given the conditions for *Bacillus* species. (f) It is also well known that diverse metabolic enzymes are operative in different cell types and governing unique functions. How, then transforming a eukaryotic cell with that of enzymes of fermentation would fit into metabolic scheme of the cell. No examples are provided of successfully manipulating various eukaryotic cell types in order to successfully reorganize the genes into the specific pathways of the individual eukaryotic cell, or reduce the accumulation of acidic metabolite, without such a guidance, the experiment left to those skilled in the art will be undue.

Applicant's Arguments :

Pointing to specification at page 14, line 2 through page 15, line 10, Applicants argue that description in detail is present of the chromosomal integration of foreign genes, in particular *Zymomonas mobilis adh* and *pdc* genes. At page 15, line 11 through page 17, line 28, the specification describe provides detailed information about how to select a suitable host, including factors to be considered in selecting a host (page 15, lines 16-19). In particular Examiner's attention is invited to page 15, lines 18-25.

Applicants' arguments are, however, not found persuasive because the scope of the claims encompass 'transforming any eukaryotic cell [which includes any animal, insect, fungal or yeast cell] with *adh* and *pdc* genes obtained from any source , hitherto undiscovered. It is further, pointed out that at the time of filing, the GenBank Data base

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had listed 5 *pdh* genes as of March, 1991 (see instant specification, page 14, lines 19-21).

As far as chromosomal integration of foreign genes is concerned, a reference (Ohta et al., 1991) is provided for chromosomal integration of ethanologenic genes in *E. coli* (page 14, last paragraph of the instant specification). However, the claims are drawn to any transformed eukaryotic cell with *adh* and *pdh* genes obtained from any source. Transforming genes into *E. coli*, or the *E. coli* expression system is well studied, as compared to expressing foreign genes into any eukaryotic cell system. Therefore the instant claims go beyond the enabling disclosure of the instant specification. The need for suitable working examples is vital for one of ordinary skill in the art in order to transform millions of diverse groups of animal cells with an equally large number of *adh* and *pdh* genes obtained from any source, and without such a guidance it will be unduly burdensome based upon the teachings of the instant disclosure, and the state of the art at the time the application was filed.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(a) Claims 1-3, 5-12 and 14-17 are rejected under the judicially created doctrine of double patenting over claims 1-2 of U. S. Patent No. **5,482,846**, since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows:

Claims 1-2 of U.S. Patent No. 5,482,846 are drawn to a species of selected gram-positive bacteria transformed with the alcohol dehydrogenase & pyruvate decarboxylase genes and method of use, as compared to any gram-positive bacteria and method of use, the genus claimed in the instant application. Since a species anticipates the genus [& genus obviates a species], the patented species claims of U.S. Patent No. 5,482,846 anticipates the instantly claimed generic claims.

Applicants' Arguments :

It is noted that the Applicants will address this issue upon indication of allowable subject matter.

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(b) Claims 1-3, 5-12 and 14-17 are rejected under the judicially created doctrine of double patenting over claims 1-2 of U. S. Patent No. 5,916,787, since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

Claims 1-18 in U.S. Patent No. 5,916,787 make the claims in the instant application obvious in expressing the heterologous genes encoding the alcohol dehydrogenase and pyruvate decarboxylase into eukaryotic cell instead of a gram +ve bacterium.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

□ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action. [see item 6b for new grounds of rejection, for example].

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (571) 272-0940. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group in the Technology Center is 703 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 571 272-1600.


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